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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,677	08/25/2003	Ashok V. Purandare	QA0259 NP	3788

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/648,677	Applicant(s) PURANDARE, ASHOK V.	
	Examiner Mark L. Berch	Art Unit 1624	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 November 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would requlre further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): All but enablement. See memo.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,2,5,6 and 8-12*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See memo. Objection to specification remains.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 11/4/2005
13. ☐ Other: _____.

Mark L. Berch
Primary Examiner
Art Unit: 1624

DETAILED ACTION

The amendment filed 11/4/2005 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance.

The references have been examined. However, the compounds are still not enabled, as applicants have not established a single utility for CCR4 antagonists.

Many of these references give only a brief mention, if any, to CCR4. At least a half a dozen make no mention of CCR4 in title, abstract or introductory paragraph. For example, Sallusto mentions CCR4 only in passing. Some references, e.g. Randolph, don't even appear to mention CCR4 at all.

In other cases, the empahsis is clearly on how much basic research is still needed. Thus, the conclusion to the Lloyd (2003) references states, ""Mouse models have generated vast amounts of data regarding the role of specific chemokines in recruiting leukocytes to the lung after allergen challenge. However. the validity of these data depends on the ability of the model to represent the human disease. Further work is needed to determine how CCR3, CCR4 and CCR8 interact to mediate the recruitment of Th2 cells and eosinophils to the allergic lung. and to confirm these results in human studies."

Discussions of therapeutic use were usually absent. When present, these were generally negative, or indicate how early this research is. Thus, the Ruth reference identified 4 receptors, one of the CCR4 but could only say, "we propose that these receptors and their respective ligands may be suitable targets for the treatment of RA" --- language which clearly indicates that such is only a possibility, not one which has been established. Others appear to point more away from CCR4 than toward it. The Krueger, Journal of the American Academy of Dermatology 46(1), Pages 1-23 (2002) reference provides an

extrensive review of potential new biological agents, yet CCR4 gets only the briefest passing notice (first column of page 11), indicating the the skill level in this art is negligible. Still others seem to explicitly downplay the improtance of CCR4. For a second example, the Lukacs paper is entitled, "Chemokine Receptors in Asthma: Searching for the Correct Immune Targets". But in the conclusion section, entitled, "Targeting chemikine receptors for attenuating airway remodeling and mucus overproduction", the focus is on CCR2. There is not even any mention of CCR4. The Figure 1 scheme on "potential activation pathways" makes no mention again on CCR4. Thus, this reference acts very much against the idea of CCR4 as being enabled as being one of the "correct immune targets" for asthma. The Biedermann seems to disparage the very approach of these claims, saying, "This implies that targeting one single chemokine receptor may not result in a sufficient blockage of Th cell migration to a certain tissue." Targeting one receptor is what the specification bases its utility on.

The one reference which most specifically discussed therapeutic use was Wakugara. Its final paragraph is as follows: "The research into chemokines and their receptors as therapeutic targets are at an early stage. Much work is needed to establish the value of this approach for future therapy. Such studies are well-justified because serum TARC levels and CCR4 expression on helper T cells are prominent features of the lesions from atopic dermatitis subjects. Therapies that are directed to chemokines and their receptors will have the potential advantage of being very selective and with fewer side effects, than the regimens that are currently available to patients with atopic dermatitis." Thus, the final paragraph makes it clear that such research is at such "an early stage" that "much work is needed to establish the value of this approach for future therapy". This is a clear statement

that, insofar as atopic dematitis is concerned, the utility is not enabled, clearly, more than just routine experimentation is needed; even the "the value of this approach for future therapy" has yet to be established.

These references taken as a whole, along with the Allen and two Barnes' references discussed previously, make it clear that such utility is not present. Applicants are urged to take one of the approaches set forth in the previous intereview.

The argument for using IC(50) rather than Ki is unpersuasive. Applicants argue that "Ki values are generally not calculated for whole cell essays". But "generally not" does not mean that it is not practical, and hence, how could one of ordinary skill in the art conclude that such was not done. Further, applicants have not provided any evidence for this assertion.

All other mattrers are resolved.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Berch
Primary Examiner
Art Unit 1624

11/23/05